

Pharmacia  
& Upjohn

Pharmaceutical Development / Oral solids and warehousing

# PROCESSING SHEET

PAGE: 1 of 45

PRODUCT:	SU 10398 (PNU-290940AD)	LOT:	I83G03	COMM.:	<u>RD000511POS ug</u>
PHARMACEUTICAL FORM:	Capsule	DOSAGE:	25 mg (as a free base)		
FORMULA No.:	83HC02	PREPARATION DATE:	<u>09/01</u>		
PROCESSING START:	<u>12/Sept./01</u>	PROCESSING FINISH:	<u>04/Oct./01</u>		
THEORETICAL QUANTITY:	<u>140000 qs</u>	(T) QUANTITY OBTAINED:	<u>125 987</u>	yield:	<u>89.3</u> %
SCOPE OF THE PREPARATION: Stability studies and clinical trial					

## THEORETICAL UNITARY FORMULA

[illegible]

**Signature of who filled out the form:**

[signature]

Approval for use by the Chief of ORAL SOLIDS and  
WAREHOUSING:

[signature]

Edition No.: 7 of 10/05/99  
Substitutes Edition No.: 6 of 03/11/97

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**Pharmaceutical Development / Oral solids and warehousing**

Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

**PRACTICAL FORMULATION**

RAW MATERIALS	CODE	LOT No.	TITER	Over dose	M.U.	PRACTICAL UNIT DOSE	M.U.	Practical quantity per ..... 140000.....
SUI0358 (PNU-290430AD)	1502	[illegible]	99.666 <sup>(A)</sup>	—	mg	33.512	g	4631.670 (B)
Mannitol NF	723	AE 130			mg	39.551	g	5537.150 (B)
Croscarmellose sodium	718	AE 112			mg	2.505	g	350.700 (B)
Povidone K25	931563000	AA10G041			mg	4.175	g	584.500 (B)
Total granulate					mg	79.743	g	11164.020
Croscarmellose sodium	718	AE 112			mg	2.505	g	350.700
Vegetable Magnesium Stearate	927406000	AA10L028			mg	1.252	g	175.280
Total					mg	83.500	g	11690.000
SHELLS Format 3—White opaque hard gelatin Head/Body								
SHELLS Format 3 Swedish orange opaque hard gelatin Head/Body	1491	AE310					N	150.000*
*ordered in excess to compensate for losses in phases of processing [initials] 12/09/01								

**NOTE:** <sup>(B)</sup> Equal to 74.6% as free base B

<sup>(B)</sup> Total Quantity – During processing these are subdivided into two loads of Granulate. B

Operator's signature: ..... [signature] .....

Verifier's signature: ..... [signature] .....

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Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

**ACTIVE PRINCIPLE: VERIFICATION OF THE PRACTICAL QUANTITY CALCULATIONS AND AVERAGE TITER**

Active principle: \_\_\_\_\_ Provided quantity: \_\_\_\_\_ A)

Lot: \_\_\_\_\_ Titer as sampled: \_\_\_\_\_

Active principle: \_\_\_\_\_ Provided quantity: \_\_\_\_\_ B)

Lot: \_\_\_\_\_ Titer as sampled: \_\_\_\_\_

Active principle: \_\_\_\_\_ Provided quantity: \_\_\_\_\_ C)

Lot: \_\_\_\_\_ Titer as sampled: \_\_\_\_\_

NOT APPLICABLE [initials] 12/09/01

Total theoretical quantity (Pt) = \_\_\_\_\_ g (Unit dose x theoretical launch quantity)

Calculated theoretical quantity (Pc) = \_\_\_\_\_ g (A x Tit. A + B x Tit. B + C x Tit. C)

Total practical quantity (Pp) = \_\_\_\_\_ g (A + B + C)

**NOTE:**1) The correspondence between the weighed active principle quantity and the practical active principle to be used is verified when  $P_t = P_c$ .This correspondence is also verified when the two values differ and the divergence between the provided quantity and the requested quantity is due exclusively to the weighted values in accordance with the divergence limits set out in procedure SF.TF 015/0 ( $\pm 0.5\%$ ).

2) If the condition in point 1) is not fulfilled, suspend the processing and inform the Lot Formation Center.

3) If the condition in point 1) is fulfilled, proceed to fill in the following points on this page.

Average titer weight =  $P_t/P_p \times 100 =$  ..... %

Active principle: \_\_\_\_\_

Quantity to use =  $P_t/\text{Titer}^* \times 100 =$  ..... g (D)

Compensation excipient: \_\_\_\_\_

Quantity to use =  $P_e - (D - P_t) =$  ..... g**NOTE:**

Pt = Weight in grams of the active principle considering a 100% titer

Pe = Compensation excipients weight in function of the active principle at 100% titer

\* = Should multiple lots be used, the titer will be the average weight, as calculated considering the quantity of each lot.

Operator's signature: \_\_\_\_\_

Verifier's signature: \_\_\_\_\_

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Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

**CLEANING OF THE EQUIPMENT AND ROOMS**

Once the processing has been completed clean the processing rooms with: See Cleaning method 50/cm019

Once the processing has been completed, clean the equipment with: See Cleaning method 50/cm019

**PROCESSING IDENTIFICATION LABELS**

**CONFORMITY VERIFICATION LABELS**

DATE: 12/09/2001

SIGNATURE: [signature]

LABELS DELIVERED

No.: 32

DATE: 17/09/2001

SIGNATURE: [signature]

ADDITIONAL DELIVERED

No.: \_\_\_\_\_

DATE: 1 / 1

SIGNATURE: \_\_\_\_\_

LABELS USED

No.: 30

DATE: 04/10/2001

SIGNATURE: [signature]

DETERIORATED LABELS

No.: \_\_\_\_\_

DATE: 1 / 1

SIGNATURE: \_\_\_\_\_

LABELS RETURNED

No.: 2

DATE: 04/10/2001

SIGNATURE: [signature]

(The returned labels are destroyed)

**LABEL MODEL**

*Pharmacia & Upjohn – Oral Solids Section*

*Pharmacia & Upjohn – Oral Solids Section*

Product: SU10398 (PNU-290940AD) Capsule 25 mg (as a free base)

**SU10398 (PNU-290940AD)**

LOT: I83G03

Prep. Date: 09/2001

FORMULA No.: 83HC02

**Capsule 25 mg (as a free base)**

Date: 12-09-2001

Label No. 16 of 16

[signature]

LOT: I83G03

Prep. Date: 09/2001

FORMULA No.: 83HC02

Gross: \_\_\_\_\_ Tare: \_\_\_\_\_ Net: \_\_\_\_\_

Date: 12/09/2001

Label No. 16 of 16

[signature]

NOTE \_\_\_\_\_

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Pharmaceutical Development / Oral solids and warehousing

Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

Room: 72

WEIGHT VERIFICATION OF  
THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 02 [init]	1	<b>Check the weight of the active principle/s</b> <i>In accordance with the indications of the procedural deviation num. 31/01, weigh out the quantity of active principle indicated below. [initials] 12/09/01</i>			
09		PRODUCT: SU 10398 (PNU-290940AD)	Lot: (B1) 6106-TSF-0101-N1		
17	1/1	LOT: (D1) 6106-TJF-0101-N1	Gross: 2562 g	[initials]	[initials]
		PRACTICAL WEIGHT 2345.835 g	Tare: 215 g		
			Net: 2347 g		
			Scale ID No.: 80-BL-35		
01		PRODUCT: SU 10398 (PNU-290940AD)	Lot: (B1) 6106-TSF-0101-N1		
09	1/2	LOT: (B1) 6106-TJF-0101-N1	Gross: 2561 g	[initials]	[initials]
18		PRACTICAL WEIGHT 2345.835 g	Tare: 215 g		
			Net: 2346 g		
			Scale ID No.: 80-BL-35		
	1/3	PRODUCT:	Lot:		
		LOT:	Gross:		
		PRACTICAL WEIGHT	Tare:		
			Net:		
			Scale ID No.:		
			[initials]		
			12/09/2001		

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Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Room: 72  
Dosage: 25 mg (as a free base)

WEIGHT VERIFICATION OF  
THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01	2	Check the weight of the following raw materials: relative to the 1 <sup>st</sup> load of granulate [initials] 12/09/01			
09	2/1	PRODUCT: <u>Mannitol NF</u>	Lot: <u>AE130</u>		
17			Gross: <u>2800.0</u> g	[initials]	[initials]
		LOT: <u>AE 130</u>	Tare: <u>30.0</u> g		
		PRACTICAL WEIGHT <u>2768.575</u> g	Net: <u>2720.0</u> g		
			Scale ID No.: <u>SO-BL-35</u>		
	2/2	PRODUCT: <u>Croscarmellose sodium</u>	Lot: <u>AE112</u>		
			Gross: <u>188.10</u> g	[initials]	[initials]
		LOT: <u>AE112</u>	Tare: <u>13.00</u> g		
		PRACTICAL WEIGHT <u>175.350</u> g	Net: <u>175.10</u> g		
			Scale ID No.: <u>SO-BL-35</u>		
	2/3	PRODUCT: <u>Povidone K25</u>	Lot: <u>AA1060A1</u>		
			Gross: <u>306.00</u> g	[initials]	[initials]
		LOT: <u>AA10G041</u>	Tare: <u>13.00</u> g		
		PRACTICAL WEIGHT <u>292.250</u> g	Net: <u>293.00</u> g		
			Scale ID No.: <u>SO-B2-35</u>		
	2/4	PRODUCT: _____	Lot: _____		
			Gross: _____ g		
		LOT: _____	Tare: _____ g		
		PRACTICAL WEIGHT _____ g	Net: _____ g		
		[initials] 12/09/01	Scale ID No.: _____		
	2/5	PRODUCT: _____	Lot: _____		
			Gross: _____ g		
		LOT: _____	Tare: _____ g		
		PRACTICAL WEIGHT _____ g	Net: _____ g		
			Scale ID No.: _____		

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Pilot Plan Formula Development  
Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 7 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01	3	<u>Preparation of the granulated solution</u>			
09	3/1	Using a sterile container, collect approximately .....150..... mL of contrast T.D.I. Water to be used and send the sample to determine its bacterial load.	T.D.I. Water Contrast No.: .....42..... mL collected: .....150.....	[initials]	[initials]
17	3/2	Weigh out .....875..... g of .....TDI H <sub>2</sub> O.....  Warm the solvent to a temperature between .....°C and .....°C and disperse under shaking:     Let it cool until a practically clear solution is obtained.  Addition of tensioactive agents <input type="checkbox"/> Weight ..... g of .....  Warm the solvent to a temperature between .....°C and .....°C and disperse under shaking:   Combine the tensioactive solution with the solution of point ..... under shaking.  [initials] 12/09 2001	Solvent Quantity Gross: .....1020..... g Tare: .....145..... g Net: .....825..... g Temperature: .....74..... °C  <input checked="" type="checkbox"/>  Solvent Quantity per Tensioactive Gross: ..... g Tare: ..... g Net: ..... g Temperature: ..... °C  [initials] 12/09 2001  <input type="checkbox"/>	[initials]	[initials]

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## Pilot Plan Formula Development

### Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 8 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	WET GRANULATION in DIOSNA	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 17	4	<p><b><u>Preliminary sieve analysis of the raw materials</u></b></p> <p>Sieve analyze the raw materials  <u>Mannitol NF</u>  <u>Croscarmellose sodium</u>  <u>Povidone K25</u>    through a _____  _____ <u>1-1.5 mm</u> _____ gauge sieve  - Equipment type: _____ <u>sieve</u> _____</p>	<p>Equipment used: _____ <u>SIEVE</u> _____</p> <p>ID number: _____ <u>—</u> _____</p> <p>Cleaning verification: _____ <u>—</u> _____</p> <p>Gauge: _____ <u>1 mm</u> _____</p>	[initials]	[initials]
01 09 17	5	<p><b><u>Mixing</u></b></p> <p>Load the raw materials from point _____ <u>1/1 and 4/1</u> _____ into the Diosna granulator and mix for _____ <u>5</u> _____ minutes under the following conditions:  Principle shaker speed: _____ <u>1</u> _____  Crusher speed: _____ <u>1</u> _____  Modify the operating conditions if necessary [initials] 12/09/01</p>	<p>ID number: _____ <u>SO-OU-04</u> _____</p> <p>Cleaning verification: _____ <u>OK</u> _____</p> <p>Principle shaker speed: _____ <u>1</u> _____</p> <p>Crusher speed: _____ <u>1</u> _____</p> <p>Start time: _____ <u>14:16</u> _____ End time: _____ <u>14:21</u> _____</p>	[initials]	[initials]
01 09 17	6	<p><b><u>Wetting</u></b></p> <p>Wet the powder with the solution prepared in point _____ <u>3</u> _____  Using a peristaltic pump <input checked="" type="checkbox"/>  Modify the operating conditions if necessary [initials] 12/09/01</p> <p>Pump capacity _____ <u>250/350</u> _____ g/min.  During the wetting employ the following conditions:  Principle shaker speed: _____ <u>1</u> _____  Crusher speed: _____ <u>1</u> _____</p>	<p>Peristaltic pump model: _____</p> <p>ID number: _____ <u>SO-OU-07</u> _____</p> <p>Cleaning verification: _____ <u>OK</u> _____</p> <p>Pump capacity _____ <u>240-260</u> _____ g/min.  Pump r.p.m. _____ <u>40-42</u> _____</p> <p>Principle shaker speed: _____ <u>1</u> _____</p> <p>Crusher speed: _____ <u>1</u> _____</p> <p>Start time: _____ <u>14:45</u> _____ End time: _____ <u>14:49</u> _____</p>	[initials]	[initials]

## Pilot Plan Formula Development

### Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 9 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	WET GRANULATION in DIOSNA	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 17	6/2	<p>If needed, add ..... <i>T.D.I. H<sub>2</sub>O</i> ..... at the end of the wetting while keeping the conditions from point ..... <i>6/1</i> ..... unchanged.</p> <p><i>Setting the most appropriate conditions. Record each added [illegible] of H<sub>2</sub>O</i></p> <p>[init] <i>12/09/01</i></p>	<p>Solvent type: ..... <i>T.D.I. H<sub>2</sub>O</i> .....</p> <p>Added quantity: ..... <i>416 g</i> .....</p> <p>T.D.I. Water contrast No.: ..... <i>42</i> .....</p> <p>Start time: ..... <i>15:05</i> ..... End time: ..... <i>15:07</i> .....</p> <p>T.D.I. Water contrast No.: .....</p> <p>mL collected: ..... <i>17-09-01</i> ..... [initials]</p>	[initials]	[initials]
01 09 17	6/3	<p>If the T.D.I. Water contrast is different from that in point ..... <i>3</i> ..... using a sterile container, collect approximately ..... <i>150</i> ..... ml of T.D.I. Water and send the sample to have its bacteria load determined.</p>	<p>T.D.I. Water contrast No.: .....</p> <p>mL collected: .....</p> <p><i>17-09-01</i> [initials]</p>		
01 09 17	7 7/1	<p><b><u>Granulation</u></b></p> <p>Proceed to the granulation of the wet mass according to the following parameters:</p> <p>Principle shaker speed: ..... <i>I/II</i> .....</p> <p>Crusher speed: ..... <i>I/II</i> .....</p> <p>Granulation time: ..... <i>At least one minute</i> .....</p> <p>*Set the condition and times so that a consolidated granulate. [initials] <i>12/09/01</i></p>	<p><i>Start time: 15:14</i></p> <p>Principle shaker speed: ..... <i>II</i> .....</p> <p>Crusher speed: ..... <i>II</i> .....</p> <p>Principle motor electricity absorption at the end of granulation: ..... <i>3.50</i> ..... A</p> <p>Granulation time: ..... <i>1'50"</i> .....</p> <p><i>End time: 15:16</i></p>	[initials]	[initials]

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Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 10 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	WET GRANULATION in DIOSNA	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01	8	<b>Drying</b>			
09	8/1	Transfer the wet granulated mass into the ..... ..... <i>GLATT GPCG5</i> ..... type dryer and dry at a relative humidity of $\leq$ 2.5 % according to the following parameters:	Equipment: ..... <i>GLATT GPCG5</i> ..... ID number: ..... <i>SO-LF-02</i> ..... Cleaning verification: ..... <i>OK</i> .....	[initials]	[initials]
17	-	<b>Heater</b> <input type="checkbox"/>			
		Temperature: ..... °C In a vacuum at <input type="checkbox"/> At an atmospheric pressure of <input type="checkbox"/>	Temperature read: ..... °C Degree of vacuum: ..... Start time: ..... End time: .....		
	-	<b>Fluid bed dryer</b> <input checked="" type="checkbox"/>			
01	8::	"AIR IN" Temperature: ..... <i>60</i> ..... °C "AIR IN" Volume: ..... * ..... Nm <sup>3</sup> /h	"AIR IN" Temperature: ..... <i>60</i> ..... °C "AIR IN" Volume: ..... <i>from 300 to 150</i> ..... Nm <sup>3</sup> /h		
09	-	Product temperature to set on the thermometric probe: ..... <i>40</i> ..... °C	Temperature set on the probe: ..... <i>40</i> ..... °C	[initials]	[initials]
17	8: 12 2 01	Time for shaking the hoses: ..... <i>~15"</i> ..... Time between hose shakings: ..... <i>3</i> ..... minutes	Time for shaking the hoses: ..... <i>15"</i> ..... Time between hose shakings: ..... <i>3</i> ..... minutes		
	-	Shaking Type WSG <input type="checkbox"/> GPCG <input checked="" type="checkbox"/>	Shaking Type WSG <input type="checkbox"/> GPCG <input checked="" type="checkbox"/>	[initials]	[initials]
		<i>*Set the air volume so as to obtain the correct movement of the product. [initials] 12/09/01</i>	Start time: ..... <i>15:38</i> ..... End time: ..... <i>16:01</i> ..... "AIR OUT" Temperature at the end of the process: ..... <i>32</i> ..... °C		

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	8/3	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks:			
	8/4	Karl Fischer: <input type="checkbox"/> until a constant weight is achieved. [initials] 12/09/01	Residual humidity: :.....1.29 %	[initials]	[initials]
	8/5	Weight loss at 110 °C for ..... min. <input checked="" type="checkbox"/>	Thermobalance at 110 °C for P.C. .... min		
	8/6	Residual humidity limit ≤ 2.5 %	Thermobalance ID number: SO-BL-42		
			Karl Fischer ID number: -		
	8/7	If the residual humidity value is not within the set limits, continue drying according to the provisions in point 8/21 <input type="checkbox"/>			
	8/8	If necessary modify:	[initials] 18/09/01		
		-the drying temperature <input type="checkbox"/>	"AIR IN" Temperature: ..... °C		
			Heater temperature: ..... °C		
	8/9	-the thermometric probe product temperature <input checked="" type="checkbox"/>	Thermometric probe product temperature: ..... °C		
			Start time: ..... End time: .....		
			"AIR OUT" temperature at the end of the process: ..... °C		
	8/10	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks again:			
	8/11	Karl Fisher: <input type="checkbox"/>	Residual humidity: :..... %		
	8/12	until a constant weight is achieved. [initials] 12/09/01	Thermobalance at ..... °C for ..... min		
	8/13	Weight loss at ..... °C for ..... min. <input checked="" type="checkbox"/>	Thermobalance ID number: .....		
		Residual humidity limit ≤ 2.5 %	Karl Fischer ID number: .....		

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Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	WET GRANULATION in DIOSNA	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	9	<b>Final Calibration</b>			
	9/1	Calibrate the dried granulated mass using <u>OSCILLATING VIANI</u> ..... ..... that is equipped with a sieve with a gauge of <u>1000</u> µm	Equipment used: ..... <u>OSCILLATING VIANI</u> ..... ID number: <u>80-95-03</u> Cleaning verification: <u>OK</u> Gauge: <u>1000</u> µm Start time: <u>9:00</u> End time: <u>9:20</u>	[initials]	[initials]
18 Sept. 01	9/2	At the end of calibration, collect the granulated mass obtained in the appropriate container/s of <u>DOUBLE PE BAG INSERTED</u> <u>into a kraft barrel</u> ..... .....	<input checked="" type="checkbox"/>	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72-69	Page: 13 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	Granulation completion

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 09 01	10	<b>Technological controls</b>			
	10/1	Sample .....50... g of granulate according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: .....50..... g		
	10/2	Apparent density (SOP SF.TF 036) <input type="checkbox"/> Limit of: <u>NOT PLANNED</u> ..... g/mL	Equipment: .....STAV 2003..... Quantity of mix used: .....50..... g V <sub>0</sub> : .....24... mL V <sub>10</sub> : .....70... mL    V <sub>500</sub> : .....52... mL V <sub>1250</sub> : .....52... mL    V <sub>2500</sub> : .....-... mL D <sub>a</sub> = .....0.626... g/mL    D <sub>i</sub> = .....0.961... g/mL	[initials]	[initials]
18 Sept. 01	10/3	Granulometry (SOP SF.TF 034) <input type="checkbox"/> Limits <u>NOT PLANNED</u> > 1000 µm: <u>CP 12/09/01</u> ..... % between 710 and 1000 µm: ..... % between 500 and 710 µm: ..... % between 250 and 500 µm: ..... % between 106 and 250 µm: ..... % < 106 µm: ..... %	Equipment: .....[illegible] 200..... Quantity of mix used: .....50..... g > 1000 µm: .....40.0 % between 710 and 1000 µm: .....10... % between 500 and 710 µm: .....15... % between 250 and 500 µm: .....17... % between 106 and 250 µm: .....37... % < 106 µm: .....21... %	[initials]	[initials]
	-	<b>Analytic controls</b>			
	-	Collect ..... (number of) granulated samples (in duplicate), according to <u>SOP SF.CF 004</u> and send them to analysis for homogeneity control.	[initials] 12/09/01 Quantity sampled: ..... g See analytical controls in process		
18 09 01	11	<b>Granulation yield control</b>	<b>Granulation obtained:</b>		
	11/1	Determine the net quantity of granulated mass obtained from the sampling for technological and analytical controls.	Gross: .....8495..... g Tare: .....3175..... g Net: .....5320..... g (D)	[initials]	[initials]
	11/2	Granulation yield % = D / theoretical	GRANULATION YIELD % = ..... (E) B 17/09/01		

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Pharmaceutical Development / Oral solids and warehousing

Product: SU 10398 (PNU-290940AD)

Lot: I83G03

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Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

Room: 72

WEIGHT VERIFICATION OF  
THE RAW MATERIALS

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	12	Check the weight of the following raw materials:			
	12/1	PRODUCT: <u>Mannitol NF</u>	Lot: <u>AE130</u>		
			Gross: <u>2799</u> g	[initials]	
		LOT: <u>AE130</u>	Tare: <u>30</u> g		[initials]
		PRACTICAL WEIGHT <u>2768.575</u> g	Net: <u>2769</u> g		
			Scale ID No.: <u>SQ-BL-35</u>		
	12/2	PRODUCT: <u>CROSCARMELLOSE SODIUM</u>	Lot: <u>AE112</u>		
			Gross: <u>189</u> g	[initials]	
		LOT: <u>AE112</u>	Tare: <u>13</u> g		[initials]
		PRACTICAL WEIGHT <u>175.350</u> g	Net: <u>[illegible]</u> g		
			Scale ID No.: <u>SQ-BL-35</u>		
	12/3	PRODUCT: <u>POVIDONE K25</u>	Lot: <u>AA10G04</u>		
			Gross: <u>305.3</u> g	[initials]	[initials]
		LOT: <u>AA10G041</u>	Tare: <u>13.0</u> g		
		PRACTICAL WEIGHT <u>292.250</u> g	Net: <u>292.3</u> g		
			Scale ID No.: <u>SQ-BL-32</u>		
		PRODUCT: _____	Lot: _____		
			Gross: _____ g		
		LOT: _____	Tare: _____ g		
		PRACTICAL WEIGHT _____ g	Net: _____ g		
			Scale ID No.: _____		
		PRODUCT: _____	Lot: _____		
			Gross: _____ g		
		LOT: _____	Tare: _____ g		
		PRACTICAL WEIGHT _____ g	Net: _____ g		
			Scale ID No.: _____		

B 12/09  
2001

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Pilot Plan Formula Development  
Oral Solids Section

Product: SU 10398 (PNU-290940AD)	Lot: 183G03	Room: 72	Page: 15 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18- Sept. 01	13	<b>Preparation of the granulated solution</b>			
	13/1	<p><i>If the contrast is different from the one in point 3 B 12/09/2001</i></p> <p>Using a sterile container, collect approximately ..... 150 ..... mL of contrast T.D.I. water to be used and send the sample to determine its bacterial load.</p>	<p>T.D.I. Water Contrast No.: ..... — .....</p> <p>mL collected: ..... — .....</p>		[initials]
	13/2	<p>Weigh out ..... 875 ..... g of ..... T.D.I. H<sub>2</sub>O .....</p> <p>Warm the solvent to a temperature between ..... °C and ..... °C and disperse under shaking:</p> <p>.....</p> <p>.....</p> <p>.....</p> <p>Let it cool until a practically clear solution is obtained.</p> <p>Addition of tensioactive agents <input type="checkbox"/></p> <p>Weight ..... g of .....</p> <p>.....</p> <p>Warm the solvent to a temperature between ..... °C and ..... °C and disperse under shaking:</p> <p>.....</p> <p>.....</p> <p>Combine the tensioactive solution with the solution of point ..... under shaking.</p>	<p>Solvent Quantity</p> <p>Gross: ..... 1020 ..... g</p> <p>Tare: ..... 145 ..... g</p> <p>Net: ..... 825 ..... g</p> <p>Temperature: ..... 74 ..... °C</p> <p><input type="checkbox"/></p> <p>Solvent Quantity per Tensioactive</p> <p>Gross: ..... g</p> <p>Tare: ..... g</p> <p>Net: ..... g</p> <p>Temperature: ..... °C</p> <p>B 12/03/01</p> <p><input type="checkbox"/></p>	[initials]	

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Oral Solids Section

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>WET GRANULATION in DIOSNA</b>			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18-Sept. 01	14	<b>Preliminary sieve analysis of the raw materials</b>			
	14/1	Sieve analyze the raw materials <i>Mannitol NF</i> <i>Croscarmellose Sodium</i> <i>Povidone</i>	Equipment used: <i>SIEVE</i> ID number: <i>I</i> Cleaning verification: <i>OK</i> Gauge: <i>[illegible]</i>	[initials]	[initials]
	14/2	through a <i>1-1.5 mm</i> gauge sieve Equipment type: <i>sieve</i>			
18-Sept. 01	15	<b>Mixing</b>			
		Load the raw materials from point <i>1/2 and 14</i> into the Diosna granulator and mix for <i>5</i> minutes under the following conditions: Principle shaker speed: <i>I</i> Crusher speed: <i>I</i> <i>Modify the operating conditions if necessary B 12/09/2001</i>	ID No.: <i>80-GU-04</i> Cleaning verification: <i>-</i> Principle shaker speed: <i>I</i> Crusher speed: <i>I</i> Start time: <i>10:00</i> End time: <i>10:05</i>	[initials]	[initials]
18-Sept. 01	16	<b>Wetting</b>			
	16/1	Wet the powder with the solution prepared in point <i>13</i> Using a peristaltic pump <input checked="" type="checkbox"/> <i>Modify the operating conditions if necessary B 12/09/2001</i> Pump capacity <i>250/350</i> g/min. During the wetting employ the following conditions: Principle shaker speed: <i>I</i> Crusher speed: <i>I</i>	Peristaltic pump model: <i>LOHER</i> ID No.: <i>80-PM-07</i> Cleaning verification: <i>-</i> Pump capacity <i>240-260</i> g/min. Pump r.p.m. <i>40-42</i> Principle shaker speed: <i>I</i> Crusher speed: <i>I</i> Start time: <i>10:25</i> End time: <i>10:30</i>	[initials]	[initials]

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	16/2	If needed, add <u>TDI H<sub>2</sub>O</u> at the end of the wetting <del>while keeping the</del> <del>conditions from point</del> <u>unchanged</u> . <i>Setting the appropriate conditions.</i> <i>Record each addition of H<sub>2</sub>O</i> [initials] 12/09/01	Solvent type: <u>TDI H<sub>2</sub>O</u> Added quantity: <u>450 S</u> T.D.I. Water contrast No.: <u>42</u> Start time: <u>10:40</u> End time: <u>10:43</u>	[initials]	[initials]
	16/3	If the T.D.I. Water contrast is different from that in point <u>13</u> , using a sterile container, collect approximately <u>50</u> ml of T.D.I. Water and send the sample to have its bacteria load determined.	T.D.I. Water contrast No.: <u>—</u> mL collected: <u>—</u>		
18 Sept. 01	17	<b>Granulation</b>  17/1 Proceed to the granulation of the wet mass according to the following parameters: Principle shaker speed: <u>I/II</u> Crusher speed: <u>I/II</u> Granulation time: <u>[illegible] 1 min.</u> <i>*Set the condition and times so that a consolidated granulate.</i> [initials] 12/09/01	START TIME: <u>10:49</u> Principle shaker speed: <u>II</u> Crusher speed: <u>II</u> Principle motor electricity absorption at the end of granulation: <u>2.50</u> A Granulation time: <u>1'</u> END TIME <u>10:50</u>	[initials]	[initials]

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	18	<b>Drying</b>			
	18/1	Transfer the wet granulated mass into the ..... GLAT GPCG 5 ..... type dryer and dry at a relative humidity of $\leq 3.5\%$ according to the following parameters:	Equipment: ..... GLAT GPCG 5 ..... ID number: ..... 80-LF-02 ..... Cleaning verification: ..... OK .....	[initials]	[initials]
	-	<b>Heater</b>  Temperature: ..... °C In a vacuum at ..... <input type="checkbox"/> At an atmospheric pressure of ..... <input type="checkbox"/>	Temperature read: ..... °C Degree of vacuum: ..... Start time: ..... End time: ..... [initials] 12/09/01		
18 Sept. 01	18/2	<b>Fluid bed dryer</b> <input checked="" type="checkbox"/>  "AIR IN" Temperature: ..... 60 ..... °C "AIR IN" Volume: ..... * ..... Nm <sup>3</sup> /h - Product temperature to set on the thermometric probe: ..... 40 ..... °C - Time for shaking the hoses: ..... ~15 sec ..... - Time between hose shakings: ..... 3 ..... minutes - Shaking Type WSG <input type="checkbox"/> GPCG <input checked="" type="checkbox"/>  *Set the air volume so as to obtain the correct movement of the product [initials] 12/09/01	"AIR IN" Temperature: ..... 60 ..... °C "AIR IN" Volume: ..... DA300A ..... Nm <sup>3</sup> /h 150 Temperature set on the probe: ..... 40 ..... °C Time for shaking the hoses: ..... 15" ..... Time between hose shakings: ..... 3 ..... minutes Shaking type WSG <input type="checkbox"/> GPCG <input checked="" type="checkbox"/>  Start time: ..... 11:10 ..... End time: ..... 11:38 ..... "AIR OUT" Temperature at the end of the process: ..... 32 ..... °C	[initials]	[initials]
18 Sept. 01				[initials]	[initials]

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	18-3-	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks:			
	18-4	Karl Fisher: <input type="checkbox"/> <i>until a constant weight is obtained</i> [initials] 12/03/01	Residual humidity: 1.97 %	[initials]	[initials]
	18-5	Weight loss at 110 °C for min. <input checked="" type="checkbox"/>	Thermobalance at 110 °C for P.C. min		
	18-6	Residual humidity limit ≤ 2.5 %	Thermobalance ID number: 80-BE-42		
	18-7	If the residual humidity value is not within the set limits, continue drying according to the provisions in point 18/2 / <input type="checkbox"/>	Karl Fischer ID number: -		
	18-8	If necessary modify:			
		-the drying temperature <input type="checkbox"/>	"AIR IN" Temperature: °C		
			Heater temperature: °C		
	18-9	-the thermometric probe product temperature <input checked="" type="checkbox"/>	Thermometric probe product temperature: °C		
			Start time: End time:		
			"AIR OUT" temperature at the end of the process: °C		
	18-10	At the end of drying, sample the granulated mass from the dryer according to the manner described in SOP SG.CF 004 and perform the following checks again:	[initials] 08/10/01		
	18-11	Karl Fisher: <input type="checkbox"/> <i>until a constant weight is obtained</i> [initials] 12/03/01	Residual humidity: %		
	18-12	Weight loss at 110 °C for min. <input checked="" type="checkbox"/>	Thermobalance at °C for min		
	18-13	Residual humidity limit ≤ 2.5 %	Thermobalance ID number:		
			Karl Fischer ID number:		

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Oral Solids Section

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Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
WET GRANULATION in DIOSNA			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	19	<b>Final Calibration</b>			
	19/1	Calibrate the dried granulated mass using <u>OSCILLATING VIANI</u> ..... ..... that is equipped with a sieve with a gauge of <u>1000</u> µm	Equipment used: ..... <u>OSCILLATING VIANI</u> ..... ID number: <u>80-G8-03</u> Cleaning verification: ..... Gauge: <u>1000</u> µm Start time: <u>11:00</u> End time: <u>11:30</u>	[initials]	[initials]
18 Sept. 01	19/2	At the end of calibration, collect the granulated mass obtained in the appropriate container/s of <u>DOUBLE PE BAG INSERTED INTO A</u> <u>KRAFT BARREL</u> .....	<input checked="" type="checkbox"/>	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72/69	Page: 21 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
Granulation completion			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	20	<b>Technological controls</b>			
	20/1	Sample .....50... g of granulate according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: .....50..... g		[initials]
	20/2	Apparent density (SOP SF.TF 036) <input checked="" type="checkbox"/> Limit of: <u>NOT</u> g/mL <u>PLANNED</u>	Equipment: <u>STAV 2003</u> Quantity of mix used: .....50..... g V <sub>0</sub> : .....78... mL V <sub>10</sub> : .....70... mL V <sub>500</sub> : .....64..... mL V <sub>1250</sub> : .....64... mL V <sub>2500</sub> : ..... mL Da = .....0.641... g/mL Di = .....0.281 g/mL	[initials]	
18 Sept. 01	20/3	Granulometry (SOP SF.TF 034) <input checked="" type="checkbox"/> Limits <u>NOT PLANNED</u> [initials] 12/09/01 <div style="border: 1px solid black; padding: 2px;">           &gt; 1000 µm: ..... %            between 710 and 1000 µm: ..... %            between 500 and 710 µm: ..... %            between 250 and 500 µm: ..... %            between 106 and 250 µm: ..... %            ≤ 106 µm: ..... %         </div>	Equipment: <u>JEL 200</u> Quantity of mix used: .....50..... g > 1000 µm: .....0... % between 710 and 1000 µm: .....1... % between 500 and 710 µm: .....9... % between 250 and 500 µm: .....9... % between 106 and 250 µm: .....34... % < 106 µm: .....52... %	[initials]	[initials]
	-	<b>Analytic controls</b>			
	-	Collect ..... (number of) granulated samples (in duplicate), according to SOP SF.CF 004 and send them to analysis for homogeneity control.	[initials] 12/09/01 Quantity sampled: ..... g See analytical controls in process		
18.09.01	21	<b>Granulation yield control</b>	<b>Granulation obtained:</b>		
		Combine: granulate from point 19/2 and 11			
	21/1	Determine the net quantity of granulated mass obtained from the sampling for technological and analytical controls:	Gross: .....8624..... g Tare: .....3133..... g Net: .....5491..... g (D)		
	21/2	Granulation yield % = $\frac{D}{\text{theoretical}} \times 100$ Theoretical = 11164.020 g [initials] 12/09/01	GRANULATION YIELD % = .....96.8..... (E) TOTAL 10811 g * (SEE NOTE)		

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 22 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	Granulation completion	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
18 Sept. 01	22-	<b>Mix preparation</b>			
	22/1	Redo the proportions and weigh the excipients listed below based on the granulation yield (E) calculated in point 21/2. Send the residual excipients to be destroyed.	<input checked="" type="checkbox"/>		
			START TIME: 15:30		
			Lot: AE112		
	22/2	Croscarmellose sodium			
		Quantity to be weighed = 350.700 g x E/100	Gross: 952.5 g		
		= 339.578 g	Tare: 13.0 g	[initials]	[initials]
		Lot: AE112	Net: 339.5 g		
			Scale ID number: SQ-136-37		
			Lot: AA10L028		
	22/3	Veg. Mg. STEARATE			
		Quantity to be weighed = 175.280 g x E/100	Gross: 102.2 g		
		= 169.671 g	Tare: 13.0 g	[initials]	[initials]
		Lot: AA10L028	Net: 169.7 g		
			Scale ID number: SQ-BL-31		
			END TIME: 16:05		
			Lot:		
		Quantity to be weighed = g x E/100 =	Gross: g		
			Tare: g		
		Lot:	Net: g		
			Scale ID number:		
			Lot:		
		Quantity to be weighed = g x E/100 =	Gross: g		
			Tare: g		
		Lot:	Net: g		
			Scale ID number:		
			Lot:		
		Quantity to be weighed = g x E/100 =	Gross: g		
			Tare: g [initials] 12/09/01		
		Lot:	Net: g		
			Scale ID number:		

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 03/3	Page: 23 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	Granulation completion	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 09 19	23 23/1	<b>Preliminary sieve analysis of the raw materials</b>  Sieve analyze the raw materials: <u>Croscarmellose sodium</u> <u>Vegetable Mg. Stearate</u>  through a <u>0.365</u> gauge sieve.	[initials] 19-09-01 Equipment used: <u>TURBULA T-50-A</u> <u>SIEVE</u> ID number: <u>SO-145-23</u> Cleaning verification: <u>OK</u> Gauge: <u>0.365 mm</u>	[initials]	[initials]
	23/2	Equipment type: <u>sieve</u>			
01 09 19	24 24/1	<b>Mixing</b>  Load the granulate from point <u>21</u> and the raw materials that fulfill the provisions of point <u>23</u> , with the exception of <u>Mg. STEARATE</u> into the <u>Turbula T50/A</u> <u>50 L Barrel</u> type mixer and mix for <u>5</u> minutes at a speed of <u>25</u> rpm.	Equipment used: <u>TURBULA</u> ID number: <u>SO-MS-23</u> Cleaning verification: <u>OK</u> r.p.m.: <u>25</u> Start time: <u>9:45</u> End time: <u>9:50</u>	[initials]	[initials]
	24/2	Add <u>Mg. STEARATE</u> to the premix described in point <u>24/1</u> and mix for <u>5</u> minutes at a speed of <u>25</u> rpm.	Start time: <u>9:55</u> End time: <u>10:00</u> r.p.m.: <u>25</u>		
	24/3	At the end of mixing, empty the mix into the appropriate container of <u>Double PE bag/Kraft Barrel</u> [initials] 12/09/01 <u>50 L STEEL BARREL</u>	<input checked="" type="checkbox"/>		

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72/69	Page: 24 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
Granulation completion			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01	25	<b><u>Technological controls</u></b>			
09	25/1	Sample .....~55 g of mix according to SOP SF.CF 004 and carry out the following controls:	Quantity sampled: .....55..... g		
19	25/2	Apparent density (SOP SF.TF 036) <input checked="" type="checkbox"/> SU 50 g Limit of: <u>NOT</u> ..... g/mL <u>PLANNED</u> [initials] 12/02 2001	Equipment: .....STAY 2003..... Quantity of mix used: .....50..... g V <sub>0</sub> : .....68..... mL V <sub>10</sub> : .....62..... mL V <sub>500</sub> : .....58..... mL V <sub>1250</sub> : .....58..... mL V <sub>2500</sub> : ..... mL Da = ..0.735..... g/mL Di = ..0.862.. g/mL L.O.D. = 1.60%		
	25/3	Run a L.O.D. check at 110°C until a constant weight is achieved [initials] 12/09/01			
	25/4	Granulometry (SOP SF.TF 034) <input type="checkbox"/> Limits > 1000 µm: ..... % between 710 and 1000 µm: ..... % between 500 and 710 µm: ..... % between 250 and 500 µm: ..... % between 106 and 250 µm: ..... % < 106 µm: ..... %	Equipment: ..... Quantity of mix used: ..... g > 1000 µm: ..... % between 710 and 1000 µm: ..... % between 500 and 710 µm: ..... % between 250 and 500 µm: ..... % between 106 and 250 µm: ..... % < 106 µm: B 12-03/2001 ..... %	[initials]	[initials]
01	25/4	<b><u>Analytic controls</u></b>			
09	25/5	Collect ..10... (number of) mix samples (in duplicate), according to SOP SF.CF 004 and send them to analysis for homogeneity control:	SINGLE SAMPLES OF 150 mg EACH Quantity sampled: .....L..... g [initials] 08/10/01 See analytical controls in process	[initials]	[initials]
01	26	<b><u>Final mix yield control</u></b>	Mix obtained:		
09	26/1	Determine the net quantity of mix obtained from the sampling for technological and analytical controls.	Gross: .....11436..... g Tare: .....168..... g Net: .....11268..... g	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 25 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	DISTRIBUTION into CAPSULES	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
20 - 09 - 01	27	<b>Distribution into capsules</b>			
	27/1	Verify the conformity of the hard gelatin shells: Format No.: .....3..... Body: <u>OPAQUE SWEDISH ORANGE</u> Head: <u>OPAQUE SWEDISH ORANGE</u> Printing: .....-..... <u>LOT No. AE310</u>	Conforms: Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> <u>LOT No. AE310</u>	[initials]	[initials]
	27/2	Weigh 100 empty shells to determine the average weight.	Average shell weight: .....48..... mg ( $\alpha$ )		
	27/3	Make the ..... .....[illegible] A25 type capsule sealing machine ready and set it to format No. ....3.... with No. ....2.... dosage dispensing. <i>format 4</i>	Capsule sealing machine: ....[illegible] A25 ID number: .....SO-OP-05..... Cleaning verification: .....OK..... Dispenser No.: .....2..... Format No.: .....4.....	[initials]	[initials]
20 - Sept - 01	27/4	Work Parameters Theoretical weight: .....83.5..... mg Distribution weight: Theoretical + $\alpha$ Weight limit: $\beta + (\pm 7.5\%$ of the theoretical)	Distribution weight: .....131.50..... mg ( $\beta$ ) Top end weight: .....137.76..... mg Bottom end weight: .....125.24..... mg	[initials]	[initials]
		Hopper level height: .....TBD..... mm Dispenser chamber height: .....TBD..... mm	Hopper level: .....30..... mm Dispenser chamber: .....10.5..... mm		
	27/5	Piston pressure Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>	Pressure index: .....-.....	[initials]	[initials]
	27/6	Teflon coated pistons Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>	Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>		
	27/7	Machine speed: .....~3500..... cps/h	Machine speed: .....3500..... cps/h Production speed: .....3500..... cps/h	[initials]	[initials]

Edition No.: 7 of 10/05/99  
Substitutes edition No.: 6 of 03/11/97

Checked by: .....[signature].....

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 26 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	DISTRIBUTION into CAPSULES	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
<u>20</u> <u>Sept.</u> <u>01</u>	27/8	During the distribution, guide the produced capsules into a cyclone separator.	Model: <u>[illegible]</u> ID number: <u>SO-SL-01</u> Cleaning verification: <u>OK</u> Operative parameters: <u>35%</u>  <u>SEE NOTE</u>	[initials]	[initials]
	27/9	As they come out of the cyclone, collect the capsules in suitable container/s of: <u>DOUBLE PE BAG / KRAFT BARREL</u>	Container used: * 20/09/01  <u>DOUBLE PE BAG /</u> <u>KRAFT BARREL</u>	[initials]	[initials]
20 - 09 - 01	28	<b><u>Sampling and controls</u></b>			
	28/1	Monitor the processing so that the process is executed within the set parameters and perform the following controls according to the manner indicated in SOP SF.CF 004 and the indications shown on the corresponding section of the form.		[initials]	[initials]
20 - 09 - 01	29	<b><u>Preparations for the sampling of the finished product for controls</u></b>			
	29/1	At the beginning, middle and end of the distribution into capsules, sample (in a manner equally spread throughout) an overall number of capsules equal to <u>~600</u> units which are necessary for controls on the finished product.	<input checked="" type="checkbox"/>	[initials]	[initials]
<u>20</u> <u>Sept.</u> <u>01</u>	30	<b><u>DISTRIBUTION START</u></b>	Date: <u>20-Sept-01</u> Time: <u>16:00</u>	[initials]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 27 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	DISTRIBUTION into CAPSULES	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
20 Sept. 01	31	<b><u>Controls while in process</u></b>			
	31/1	Capsule appearance at the beginning of distribution (that there are no signs of rupture or crushing on the body and/or tips)	Capsule appearance at the beginning of distribution ... <u>CONFORMS</u> .....	[initials]	[initials]
	31/2	Uniformity of weight/average weight (SOP SF.CI 051)	<input checked="" type="checkbox"/>		
	31/3	Disintegration (SOP SF.CI 015)	<input checked="" type="checkbox"/>		
	-	<del>Uniformity of contents <input type="checkbox"/></del> (sample 30 capsules at the beginning – middle – end of distribution and send the samples to SF/Pharmaceutical Controls)	<del>Beginning <input type="checkbox"/></del> <del>Middle <input type="checkbox"/></del> <del>End <input checked="" type="checkbox"/> [initials] 13/09/01</del>		
20 02 01	31/4	Capsule appearance at the end of distribution (that there are no signs of rupture or crushing on the body and/or tips)	Capsule appearance at the end of distribution ..... <u>CONFORMS</u> .....	[initials]	[initials]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 28 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

**IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)**

Scale model: SARTORIUS		ID number: SO - BL - 37											
Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations								
Start/End of processing/day and every 30 min	131.50 mg	137.76 mg	125.24 mg	20	31/2								
DATE	TIME	SINGLE WEIGHT VALUES								AVG	S.D.	CV%	
20 Sep 01	16:00									131.9	30	1.52	
	16:30	(illegible)								131	1.6	1.22	
	17:00									131.7	1.1	0.89	
21 Sept 01	09:30									131.1	0.9	0.69	
	10:00									130.3	0.8	0.61	
	10:30									131.3	1.3	0.99	
	11:00									131	1.3	0.99	
	11:30									131.1	1.1	0.84	
	12:00									131.7	1.3	0.99	
24 Sep 01	09:10									130.7	1.1	0.84	
	09:40									132.9	1.4	1.05	
	10:10									133	1.5	1.13	
	10:40									132.6	1.8	1.37	
	11:10						M	D.S.	CV%	132.0	1.1	1.29	
	11:40	MACHINE TIME STOPPED. RESTARTED 11:58 (SEE (illegible))								131.8	1.3	0.99	
	13:30									132.8	1.2	0.90	
	14:00									133.2	1.4	1.05	
	14:30									132.8	1.5	1.13	
	15:00									133.0	1.6	1.20	
	15:30									133.1	1.1	0.83	
	16:00									133.1	1.7	1.28	
	16:30									132.7	1.6	1.21	
25-09-01	9:30									130.1	2.0	1.53	
	10:00									131.5	1.8	1.37	
	10:30									133.3	2.0	1.50	
MACHINE STOPPED													
START (illegible)	25/09/01	13:15	STOP										25-09-01 [initials]

24.9.2001  
[signature]

OPERATOR'S SIGNATURE: [signature]	VERIFIER'S SIGNATURE: [signature]
Edition No.: 7 of 10/05/99 Substitutes edition No.: 6 of 03/11/97	Checked by: [signature]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 29 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

**IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)**

Scale model: <u>SARTORIUS</u>		ID number: <u>SO - BL - 37</u>									
Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations						
Start/End of processing/day and every .....30 min.....	131.50 mg	137.76 mg	125.24 mg	20	31/2						

DATE	TIME	SINGLE WEIGHT VALUES							AVG	S.D.	CV%		
25-03-2001	13:30								131.9	1.3	0.99		
	14:00								131.8	1.1	1.29		
STOP	14:30								132.6	1.6	1.21		
26-9-01	10:15						M	D.S.	CV%	131.7	1.3	0.99	
STOP	10:45						132.0	1.5	1.19	<del>131.4</del>	<del>3.2</del>	<del>2.44</del>	
	11:30	RESTART AFTER BRIEF STOP OF THE MACHINE [initials] 26/04/01									132.2	1.8	1.36
STOP	12:00								131.3	1.6	1.23		
26/9/01	13:30	MACHINE ADJUSTMENT AND STOP [initials] 21/09/01 TIME 14:59									131.1	1.5	1.14
26/9/01	16:20	RESTART AFTER STOP FOR ADJUSTMENT [initials] 26/09/01									130.8	0.8	0.61
26/9-01	16:50								131.3	1.8	1.37		
27-09-01	08:30								130.5	<del>3.1</del> 3.6	1.58		
	09:00								131.3	1.2	0.91		
	09:30								133.1	1.1	1.28		
	10:00	MACHINE STOP		[initials] 27/09/01							132.4	1.9	1.66
	11:00								132.7	1.3	0.98		
	11:30								134.3	1.3	0.97		
	12:00								133.3	1.2	0.90		
	12:30								133.3	1.8	1.35		
	13:00								132.2	1.6	1.21		
	13:30								133	1.7	1.28		
	14:00								133.6	1.8	1.35		
	14:30								133.9	1.9	1.05		
	15:00								131.5	1.4	1.06		
	15:30								132.5	1.3	0.98		
	16:00	MACHINE STOP		21 May 01 [signature]									
	16:15								132.1	1.4	1.06		
27-SEP-01	16:45								132.1	1.4	1.06		
28-09-2001	08:10								131.7	1.9	1.44		

26-09-2006  
signature

OPERATOR'S SIGNATURE: .....[signature].....

VERIFIER'S SIGNATURE: .....[signature].....

Edition No.: 7 of 10/05/99  
Substitutes edition No.: 6 of 03/11/97

Checked by: .....[signature].....

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 30 of 45
Pharmaceutical form: Capsule			Dosage: 25 mg (as a free base)
<b>DISTRIBUTION into CAPSULES</b>			

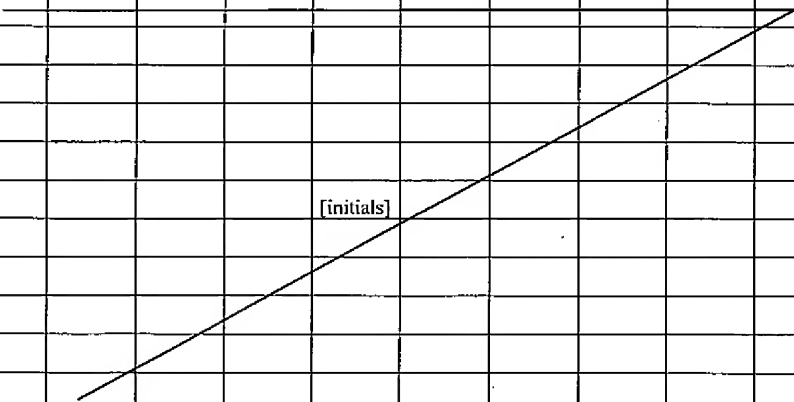
### IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051) \* SEE NOTES 01/10/01

Scale model: <u>SARTORIUS</u>		ID number: <u>SO - BL - 37/31</u>												
Frequency	Avg. theoretical weight	Top end weight	Bottom end weight	No. controls per insp.	No. of Operations									
Start/End of processing/day and every .....30 min.....	131.50 mg	137.76 mg	125.24 mg	20	31/2									
DATE	TIME	SINGLE WEIGHT VALUES										AVG	S.D.	CV%
28-09-2001	08:35											131.0	2.1	1.60
	09:05											131.7	1.8	1.37
	09:35											132.2	1.7	1.29
	10:05											133.5	1.8	1.36
	10:35											132.9	1.6	1.20
	11:05											131.2	1.7	1.30
	11:35											131.8	1.2	0.91
	12:05											132.2	1.4	1.06
	12:35											132.9	1.5	1.13
	13:05											132.7	2.0	0.68
	13:35											133.3	1.5	1.13
	14:05											132.8	1.6	1.2
	14:35											132.5	1.5	1.13
	15:05											132.3	1.8	1.36
	15:35											132.1	1.5	1.14
01-10-2001	08:35											132.6	2.0	1.51
	09:01											131.5	1.2	0.91
	09:30	132	134	134	131	131	131	133	133	130	130	131.8	1.3	1.00
		132	131	130	133	133	133	131	130	132	132	132.4	1.4	0.83
	10:00											132.4	1.1	0.83
	10:30											132.1	0.9	0.72
	11:00											133	1.2	0.88
	11:30											133.3	1.3	0.95
	12:00											133.2	1.5	1.10
	12:30											133.2	1.3	0.96
	13:00											132.4	1.5	1.13
	13:30											134	1.3	0.98
	14:00											133.3	1.4	1.06

OPERATOR'S SIGNATURE: _____ [signature]	VERIFIER'S SIGNATURE: _____ [signature]
Edition No.: 7 of 10/05/99 Substitutes edition No.: 6 of 03/11/97	Checked by: _____ [signature]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 31 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	DISTRIBUTION into CAPSULES	

**IN PROCESS WEIGHT CONTROLS (SOP SF.CI 051)**

Scale model: SARTORIUS		ID number: SO - BL - 31												
Frequency		Avg. theoretical weight		Top end weight		Bottom end weight		No. controls per insp.		No. of Operations				
Start/End of processing/day and every 30 min.....		131.50 mg		137.76 mg		125.24 mg		20		31/2				
DATE	TIME	SINGLE WEIGHT VALUES										AVG	S.D.	CV%
01-Oct-01	14:30											132.1	1.4	1.07
	15:00											132.6	1.3	0.99
	15:30											131.7	1.3	1.02
	16:00	MACHINE STOP		[initials]										
	16:20											131.5	1.5	1.14
	16:50											133	1.5	1.14
02-10-01	08:20											130.6	1.8	1.41
	08:50											130.5	1.6	1.23
	09:20											131.6	1.9	1.42
	09:50											131.9	1.6	1.23
	10:10	Machine Stop		[initials]										
	10:40											133	1.0	0.75
	11:10											131.5	1.8	1.36
END	11:40											130.9	1.2	0.94
														

OPERATOR'S SIGNATURE: [signature]

VERIFIER'S SIGNATURE: [signature]

Edition No.: 7 of 10/05/99  
Substitutes edition No.: 6 of 03/11/97

Checked by: [signature]

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72/69	Page: 32 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

**IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)**

EQUIPMENT: <u>SOTAX</u>		<u>DT 3</u>		ID number: <u>SO - DG - 01</u>					
FREQUENCY		LIMITS	IMMERSION FLUID			No. controls per inspection	No. OPERATIONS		
Start/End of processing/day and every <u>1</u> hours		≤ <u>30</u> min	<u>TDI H2O</u>			6	31/3		
DATE	TIME	CONTROLS ON IMMERSION FLUID		SINGLE VALUES					
20 Sept. 01	16:00	Temp: <u>37</u> °C Level: <u>Conforms</u>		6'00"	6'30"	6'59"	7'00"	2'30"	7'50"
20 Sept. 01	12:00	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		3"	3'20"	3'30"	7'40"	3'50"	4'10"
21 Sept. 01	9:30	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		4'18"	5'00"	5'30"	6'00"	6'30"	7'40"
21 Sept. 01	12:00	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		4'50"	5'10"	5'30"	5'40"	6'20"	7'30"
24 Sept. 01	09:10	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		5'30"	5'50"	6'10"	6'50"	7'30"	8'00"
24 Sept. 01	13:10	Temp: <u>37.4</u> °C Level: <u>Conforms</u>		4'00"	5'50"	6'30"	7'10"	7'30"	7'50"
24 Sept. 01	16:30	Temp: <u>37.4</u> °C Level: <u>Conforms</u>		5'00"	6'20"	6'40"	6'50"	3'00"	7'10"
25-09-01	9:30	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		4'25"	5'00"	5'15"	[illegible] 6'50" 6'50"	6'55"	7'20"
25-09-01	13:35	Temp: <u>37.4</u> °C Level: <u>Conforms</u>		5'10"	5'50"	6'10"	6'25"	7'00"	7'35"
25-09-01 [illegible] 26-09-01 STOP	14:30 15:15 [illegible]	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		4'55"	5'10"	5'15"	6'15"	6'50"	7'10"
26-09-01 *SEE NOTE	10:16	Temp: <u>37.5</u> °C Level: <u>Conforms</u>		5'25"	5'45"	6'25"	6'50"	7'10"	7'20"
27 Sept. 01	08:30	Temp: <u>37.4</u> °C Level: <u>Conforms</u>		5'10"	5'50"	6'10"	6'50"	7'20"	7'50"

OPERATOR'S SIGNATURE: .....[signature].....

VERIFIER'S SIGNATURE: .....[signature].....

Edition No.: 7 of 10/05/99  
Substitutes edition No.: 6 of 03/11/97

Checked by: .....[signature].....

Pharmacia  
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Pharmaceutical Development / Oral Solids and Warehousing

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72-69	Page: 33 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

**IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)**

EQUIPMENT: <u>SOTAX DT 3</u>		ID number: <u>SO-DG-01</u>						
FREQUENCY		LIMITS	IMMERSION FLUID			No. controls per inspection	No. OPERATIONS	
Start/End of processing/day and every <u>1</u> hours		≤ <u>30</u> min	<u>TDI H2O</u>			<u>6</u>	<u>31/3</u>	
DATE	TIME	CONTROLS ON IMMERSION FLUID	SINGLE VALUES					
22 Sept. 01	12:30	Temp: <u>37.4</u> °C Level: <u>Conforms</u>	6'00"	6'50"	7'10"	8'00"	8'30"	8'50"
22 Sept. 01	16:45	Temp: <u>37.4</u> °C Level: <u>Conforms</u>	5'50"	6'20"	6'50"	7'00"	7'20"	7'40"
28/09/01	8:30	Temp: <u>36.8</u> °C Level: <u>Conforms</u>	7'30"	8'30"	9'10"	9'30"	9'35"	9'40"
28/Sept/01	12:30	Temp: <u>37.2</u> °C Level: <u>Conforms</u>	6'50"	7'20"	7'40"	7'50"	8'00"	8'30"
28/Sept/01	15:35	Temp: <u>37.4</u> °C Level: <u>Conforms</u>	7'00"	7'20"	3'50"	8'10"	8'40"	9'00"
01/Oct/01	08:45	Temp: <u>37.4</u> °C Level: <u>Conforms</u>	5'10"	5'30"	5'50"	6'20"	7'30"	7'50"
01/Oct/01	12:45	Temp: <u>37.4</u> °C Level: <u>Conforms</u>	6'40"	6'50"	7'10"	7'30"	7'50"	8'10"
01/Oct/01	16:50	Temp: <u>37</u> °C Level: <u>Conforms</u>	6'10"	7'50"	8'30"	8'50"	9'00"	9'20"
02/10/01	8:40	Temp: <u>36.8</u> °C Level: <u>Conforms</u>	6'30"	6'45"	7'30"	8'05"	8'45"	10'30" CPS that floats [initials] 2/10-01
02/Oct/01	11:40	Temp: <u>37.2</u> °C Level: <u>Conforms</u>	7'00"	7'20"	7'50"	8'00"	8'15"	9'20"
		Temp: _____ °C Level: _____	[initials]					
		Temp: _____ °C Level: _____						

OPERATOR'S SIGNATURE: _____ [signature]	VERIFIER'S SIGNATURE: _____ [signature]
Edition No.: 7 of 10/05/99 Substitutes edition No.: 6 of 03/11/97	Checked by: _____ [signature]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: _____	Page: <u>34</u> of <u>45</u>
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	<b>DISTRIBUTION into CAPSULES</b>	

**IN PROCESS DISINTEGRATION CONTROLS (SOP SF.CI 015)**

EQUIPMENT: _____		ID number: _____			
FREQUENCY		LIMITS	IMMERSION FLUID	No. controls per inspection	No. OPERATIONS
Start/End of processing/day and every ..... hours.....		≤ <u>30</u> min	<i>TDI H<sub>2</sub>O</i>	<u>6</u>	<u>31/3</u>
DATE	TIME	CONTROLS ON IMMERSION FLUID		SINGLE VALUES	
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C	[initials]		
		Level: _____	<u>5/10/01</u>		
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			
		Temp: _____ °C			
		Level: _____			

OPERATOR'S SIGNATURE: \_\_\_\_\_

VERIFIER'S SIGNATURE: \_\_\_\_\_

Edition No.: 7 of 10/05/99  
Substitutes edition No.: 6 of 03/11/97

Checked by: \_\_\_\_\_

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72	Page: 35 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
2 Oct. 01	32	<b>END OF DISTRIBUTION</b>	Date: 02-04-01 Time: 11:40	[signature]	[signature]
02-03 Oct 01	33	<b>Controls on the finished product</b>			
	33/1	Using the capsules sampled in point 29, prepare and carry out the following samples:			
	33/2	No.: 106 for section controls	No.: 106		
	33/3	No.: 50 for chemical controls	No.: 50	[signature]	[signature]
	33/4	No.: 30 for dissolution and possible technological controls by SF/Pharmaceutical Controls	No.: 30		
	33/5	No.: 310 for bacterial loads (40g)	No.: 310 (40g)		
	33/6	No.: — for —	No.: —		
02-03 Oct 01	34	<b>Section technological controls</b>			
	34/1	Perform the following section controls and report the data on the appropriate section regarding the FINISHED PRODUCT <input checked="" type="checkbox"/>  DURING PROCESSING <input type="checkbox"/>	Data reported on: FINISHED PRODUCT <input checked="" type="checkbox"/> DURING PROCESSING <input type="checkbox"/>	[signature]	[signature]
	34/2	Uniformity of weight/average weight (SOP SF.CI 051)	<input checked="" type="checkbox"/>		
	34/3	Disintegration (SOP SF.CI 015)	<input checked="" type="checkbox"/>		

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 72/69 53	Page: 36 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	DISTRIBUTION into CAPSULES	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
07 Oct. 01	35	<b><u>Analytical controls on the finished product</u></b>		[initials]	[initials]
	35/1	Send the above taken samples for the execution of the following controls and fill in the appropriate section regarding the: IN PROCESS ANALYTIC CONTROLS <input type="checkbox"/>  SENDING FOR FINISHED PRODUCT ANALYSIS <input checked="" type="checkbox"/>	Data reported on: IN PROCESS ANALYTIC CONTROLS <input type="checkbox"/> SENDING FOR FINISHED PRODUCT ANALYSIS <input checked="" type="checkbox"/>		
	35/2	Titer <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/3	Correlated substances <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/4	Uniformity of content <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/5	Karl Fisher <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/6	Uniformity of weight <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/7	Dissolution <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/8	Bacterial load <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
	35/9	Other: <u>IDENTIFICATION</u> <input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>		
3-10-01	36-	<b><u>Metal detector control</u></b>	OPERATIONS PERFORMED ROOM 53		
	36/1	At the end of the distribution, pass the suitable capsules through the metal detector	Model: <u>PRISMA</u> ID number: <u>SO/AT/02</u> Cleaning verification: <u>O.K.</u> Operative parameters: <u>SENSITIVITY PROGRAM</u>	[signature]	[signature]
	36/2	Verify the number of capsules discarded at the end of the operation	Discarded capsules: Gross: .....g Tare: .....g Net: .....g Equal to ..... (number) capsules as calculated based on the average weight	[signature]	[signature]
	36/3-	Take care to send the discarded capsules to be destroyed.	<input checked="" type="checkbox"/>		
4-10-01					

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**Pharmaceutical Development / Oral Solids and Warehousing**

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: 37 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

**IN PROCESS ANALYTICAL CONTROLS**

OPER. No.	DATE	SAMPL E No.	Numeric or ponderal quantity	CONTROL TYPE	LABORATORY	RESPONSE No. and DATE	OPERATOR	VERIFIER
3/1	17.09. 01	1	150 ul	BACTERIAL LOAD CONTRAST H <sub>2</sub> O 42	microbiologica I [illegible]	200071017 25/09/01	[initials]	[initials]
25/5	19-09-01	10	2g	MIX HOMOGENEITY	AD5	20012723 24/09/01	[initials]	[initials]

**TO SEND TO FINISHED PRODUCT ANALYSIS**

DATE	Numeric or ponderal quantity	CONTROL TYPE	LABORATORY	RESPONSE No. and DATE	OPERATOR	VERIFIER
03-Oct-01	50 [initials]	CHEMICAL CONTROLS	ANALYTICAL ADS	20013158 13/11/01	[initials]	[initials]
03-Oct-01	30 [initials]	DISSOLUTION AND EV.	ANALYTICAL ADS	20013158 13/11/01		
07-Oct-01	310 [initials]	BACTERIAL LOAD	BIOLAB [initials] 10.10.01 ANALYTICAL ADS	20013158 13/11/01		

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Checked by: \_\_\_\_\_

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## TECHNOLOGICAL CONTROLS ON THE FINISHED PRODUCT

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Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: <u>39</u> of <u>45</u>
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

**TECHNOLOGICAL CONTROLS ON THE FINISHED PRODUCT**

DATE	CONTROL	LIMITS/REFERENCES	RESULT	OPERATOR	VERIFIER						
<u>02-</u> <u>Oct</u> <u>01</u>	<b>AVERAGE WEIGHT</b> SOP SF.CI 048	Theoretical: <u>131.50</u> mg Minimum: <u>128.37</u> mg Maximum: <u>136.63</u> mg	Average: <u>132.3</u> mg S.D.: <u>1.2</u> C.V.%: <u>1.31</u>	[initials]	[initials]						
<u>02-</u> <u>Oct</u> <u>01</u>	<b>DISINTEGRATION</b> SOP SF.CI 015	Limit: <u>&lt;30'</u> Immersion fluid: <u>WATER 7D1 37°C</u>  Disks: Yes <input type="checkbox"/> No <input checked="" type="checkbox"/>	Disintegrator: <u>SOTAX DT3</u> ID No.: <u>SO / DG / 01</u> Immersion fluid: <u>TDI H<sub>2</sub>O</u>  Temperature: <u>37.4</u> °C Liquid level: <u>Conforms</u> Disks: Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> <table border="1"> <tr> <td><u>6'50"</u></td> <td><u>7'20"</u></td> <td><u>7'50"</u></td> </tr> <tr> <td><u>8'10"</u></td> <td><u>8'30"</u></td> <td><u>8'55"</u></td> </tr> </table>	<u>6'50"</u>	<u>7'20"</u>	<u>7'50"</u>	<u>8'10"</u>	<u>8'30"</u>	<u>8'55"</u>	[initials]	[initials]
<u>6'50"</u>	<u>7'20"</u>	<u>7'50"</u>									
<u>8'10"</u>	<u>8'30"</u>	<u>8'55"</u>									
	<b>LOSS OF WEIGHT</b> SOP SF.CI 029	Limit: _____ Temperature: _____ °C Time: _____	Equipment: _____ ID No.: _____ / _____ / _____ Temperature: _____ °C Time: _____ minutes Loss of weight: _____ %								
	<b>FRIABILITY</b> SOP SF.CI 025	Quantity for the control: _____	Friabilimeters: _____ ID No.: _____ / _____ / _____ Initial weight: _____ g Final weight: _____ g Friability: _____ %								

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Checked by: \_\_\_\_\_ [signature]

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[initials] 40

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 53	Page: 39 of 45
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)	
<b>DISTRIBUTION into CAPSULES</b>			

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER										
3-10-2001	37	<b>Processing yield controls</b>													
	37/1-	At the end of the processing collect the capsules and place them in the following primary packaging:  <u>DOUBLE PE BAG / KRAFT BARREL</u>	Primary packaging used:  <u>DOUBLE PE BAG /</u> <u>KRAFT BARREL</u>												
	37/2	Determine the quantity of product obtained in ponderal terms.	<table border="1"> <tr> <td><u>Ponderal yield:</u></td> <td>[initials] 4-10-01</td> </tr> <tr> <td><u>BARREL 1</u></td> <td><u>BARREL 2</u> <u>BARREL 3</u></td> </tr> <tr> <td>Gross: <u>10.00 kg</u></td> <td><u>11344 g</u> <u>13045</u></td> </tr> <tr> <td>Tare: <u>2.850 kg</u></td> <td><u>3003 g</u> <u>2838</u></td> </tr> <tr> <td>Net: <u>7.150 kg</u></td> <td><u>8341 g(H)</u> <u>8-2-08</u></td> </tr> </table> <p>[initials] 4-10-01</p> <p>NOTE: The weighing will be performed direct at the end of the sorting, and parallel-channeled into the capsule sealing phase. [initials] [illegible]</p>	<u>Ponderal yield:</u>	[initials] 4-10-01	<u>BARREL 1</u>	<u>BARREL 2</u> <u>BARREL 3</u>	Gross: <u>10.00 kg</u>	<u>11344 g</u> <u>13045</u>	Tare: <u>2.850 kg</u>	<u>3003 g</u> <u>2838</u>	Net: <u>7.150 kg</u>	<u>8341 g(H)</u> <u>8-2-08</u>	[signature]	[signature]
<u>Ponderal yield:</u>	[initials] 4-10-01														
<u>BARREL 1</u>	<u>BARREL 2</u> <u>BARREL 3</u>														
Gross: <u>10.00 kg</u>	<u>11344 g</u> <u>13045</u>														
Tare: <u>2.850 kg</u>	<u>3003 g</u> <u>2838</u>														
Net: <u>7.150 kg</u>	<u>8341 g(H)</u> <u>8-2-08</u>														
	37/3	Calculate the numeric quantity of the obtained product:													
	37/4	Numeric yield = H / average weight <sup>(*)</sup>	<u>Numeric yield:</u> <u>16549</u> = No. _____ (G)												
	37/5	(*) Obtained by final controls	[initials] 04/10/01	[signature]	[signature]										
		End of processing yield: (G / THEORETICAL <sup>(*)</sup> ) * 100 (*) T from page 1 (140000 qs)	<u>% Yield:</u> _____ = _____ % The final yield is calculated after the sorting. [initials] 04/10/01												
04-10-2001	38	Calculate the mix quantity and residual shells and see to:  SENDING THE MIX AND SHELLS TO BE DESTROYED <input checked="" type="checkbox"/> SET ASIDE THE MIX <input type="checkbox"/> NOTE: _____	<table border="1"> <tr> <td><u>Residual mix</u></td> <td><u>Residual shells</u></td> </tr> <tr> <td>Gross: <u>260</u> g</td> <td>Gross: <u>600</u> g</td> </tr> <tr> <td>Tare: <u>20</u> g</td> <td>Tare: <u>120</u> g</td> </tr> <tr> <td>Net: <u>240</u> g</td> <td>Net: <u>480</u> g</td> </tr> </table> SENT TO BE DESTROYED <input checked="" type="checkbox"/> SET ASIDE <input type="checkbox"/>	<u>Residual mix</u>	<u>Residual shells</u>	Gross: <u>260</u> g	Gross: <u>600</u> g	Tare: <u>20</u> g	Tare: <u>120</u> g	Net: <u>240</u> g	Net: <u>480</u> g	[signature]	[initials]		
<u>Residual mix</u>	<u>Residual shells</u>														
Gross: <u>260</u> g	Gross: <u>600</u> g														
Tare: <u>20</u> g	Tare: <u>120</u> g														
Net: <u>240</u> g	Net: <u>480</u> g														

Product: SU 10398 (PNU-290940AD)	Lot: 183G03	Page: 41 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01/10/01  1-4-10-01	39  39/1	<p><u>Sorting the lot</u></p> <p>[initials] [illegible] 01/10/01</p> <p>Proceed to the sorting of the sample as described in the following section. At the end of processing, collect a number of samples equal to 3% of the numeric yield of the lots at the end of processing, from various points in the bulk. Report the results on the corresponding page.</p> <p><i>IN ORDER TO ELIMINATE THE CAPSULES MARKED BY THE CAPSULE SEALER PROCEED WITH THE UNIT SORTING OF THE [illegible] SAMPLE CAPSULES WHICH HAVE BEEN PRODUCED AND DEPOWDERED. START THE PARALLEL SORTING IN THE FINAL SEALING PHASE.</i></p> <p>SEE NOTE. [initials] 01/10/01</p>	Quantity sampled: No. <u>                    </u>	[initials]	[initials]

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Page: 42 of 45
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)	

**SORTING of the SAMPLES from the PRODUCT OBTAINED at the END OF PROCESSING**

PHARMACEUTICAL FORM: CAPSULE QUANTITY OBTAINED: No. ....(A) QUANTITY to be SORTED: No. ....(B) [Equal to 3% of A] SORTING LIMITS – PRIMARY DEFECTS: NOT MORE than THREE UNITS APPEARANCE: _____ _____ _____						
	DATE	DATE	DATE	DATE	DATE	DATE
LIST OF PRIMARY DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
CAPSULES BROKEN ON THE TIPS						
CAPSULES BROKEN ON THE BODY						
BODY IS VISUALIZED ON THE HEAD						
TOTAL [initials]	5/10/01					
LIST OF SECONDARY DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
TOTAL						
NOTE: _____ _____ _____						

Operator's signature	Verifier's signature	Checked by:
----------------------	----------------------	-------------

<b><u>APPEARANCE CONFORMITY</u></b>	
LOT CONFORMS for APPEARANCE	<input type="checkbox"/>
LOT DOES NOT CONFORM for APPEARANCE go to UNIT SORTING	<input type="checkbox"/>
SECTION CHIEF SIGNATURE: _____	

Pharmaceutical Development / Oral Solids and Warehousing

Product: SU 10398 (PNU-290940AD)	Lot: I83G03	Room: 54	Attachment No.: 1 page 42
Pharmaceutical form: Capsule	Dosage: 25 mg (as a free base)		

SORT TYPE:

MANUAL ☒

WITH A SORTER ☐

SORTER MODEL:

CLEANING VERIFICATION:

	DATE 1-10-2001	DATE 2-10-01	DATE 3-10-01	DATE 4-10-01	DATE	DATE
LIST OF DEFECTS	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES	NO. OF PIECES
CAPSULES BROKEN ON THE TIPS						
CAPSULES BROKEN ON THE BODY						
BODY IS VISUALIZED ON THE HEAD	75	220	36	0		
CAPSULES CRUSHED AT TIPS						
CAPSULES WITH DOUBLE BODY OR DOUBLE HEAD	10	35	2	0		
					[initials] 4-10-01	
PARTIAL TOTAL	85	255	38	0		

FINAL BALANCE

QUANTITY TO BE SORTED:

(K)

TOTAL SORTED OUT TO BE DISCARDED:

378 [initials]

(Y)

TOTAL SORTED INTO SELECTION:

(X)

X= K-Y

NOTE: K = Processing end yield – sample sorted out to be discarded

THE WEIGHING, MADE IN PROCESS, WILL BE PERFORMED AT THE END OF THE SORTING WORK AND ARE TO BE VERIFIED BY A METAL DETECTOR.

[initials] 01/10/2001

NOTES: On the 1<sup>st</sup> and 2<sup>nd</sup> of October capsules sorted from production with mealine with technical problems!

The production root setting is correct and has been unit sorted despite the fact the capsules with anomalies or broken have now been diminished.

[initials] 2/10/2001

Operator's signature: \_\_\_\_\_ [signature]

Verifier's signature: \_\_\_\_\_ [signature]

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**Substitutes edition No.: 6 of 03/11/97**

Checked by: \_\_\_\_\_ [signature] \_\_\_\_\_

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Product: SU 10398 (PNU-290940AD)		Lot: I83G03		Page: 43 of 45	
Pharmaceutical form: Capsule		Dosage: 25 mg (as a free base)			
DATE	OPER. No.	OPERATION DESCRIPTION	PRODUCTION DATA	OPERATOR	VERIFIER
01 10 01	39/2	If the results of the sampling sorting are outside the set limits, proceed to unit sorting of the lot as described in the attached form. <i>NOTE: THE UNIT SORTING IS DIRECTLY DONE IN ORDER TO ELIMINATE THE DEFECTIVE CAPSULES (THOSE MARKED ON THE TOP) CAUSED BY TECHNICAL DIFFICULTIES WITH THE CAPSULE SEALER. [initials] 01/10/01</i>	<input type="checkbox"/>		
	39/3	At the end of the sorting operation, send the discarded product to be destroyed.	<input checked="" type="checkbox"/>	[signature]	[signature]
3-10-01	40	<b>Counter sampling</b>			
	40/1	Sample <u>100</u> (number) units and package them in: <u>PE BOTTLES</u>	Quantity sampled: No. <u>100</u> <input checked="" type="checkbox"/> SEE NOTE [initials] 08/10/01	[signature]	[initials]
4-10-01	41	<b>Final lot yield control</b>	<i>THE WEIGHTS HAVE BEEN PROVIDED HERE AS SUMS OF THOSE RELATIVE TO THE TWO PARTS</i> Available product <u>SEE NOTES (END SUM)</u>		
	41/1	Proceed to the quantitative verification of the available product.	Gross: <u>22390</u> g [initials] 4/10/2001 Tare: <u>5841</u> g Net: <u>16549</u> g (U)	[signature]	[initials]
	41/2	Numeric yield = U / average weight <sup>(*)</sup> (*) Taken from the final controls	Numeric yield = <u>125087</u> (V)		
	41/3	% Yield = (V / THEORETICAL <sup>(*)</sup> ) * 100 (*) T of page 1	% Yield: <u>89.3</u> (Z)		
4-10-01	42	<b>Deposit in the warehouse</b>			
	42/3	Load the finished product and the counter sample into the SF/Warehouse, stocking them as: <u>T.A.</u>	<input checked="" type="checkbox"/>	[signature]	[initials]

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Checked by: \_\_\_\_\_ [signature] \_\_\_\_\_

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Product: SU 10398 (PNU-290940AD)

Lot: I83G03

Page: 45 of 45

Pharmaceutical form: Capsule

Dosage: 25 mg (as a free base)

**LOT APPROVAL**

**OPERATIVE VERIFICATION of the "ORAL SOLIDS" SECTION**

NOTES: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

SIGNATURE: \_\_\_\_\_ [signature] \_\_\_\_\_ DATE: 08/10/2001

**CHIEF of "ORAL SOLIDS and WAREHOUSING" APPROVAL**

RESULTS: APPROVED ☒ REJECTED ☐

NOTES: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

SIGNATURE: \_\_\_\_\_ [signature] \_\_\_\_\_ DATE: 13/11/2001

**USE AUTHORIZATION OF THE CHIEF of "Q.C./PHARMACEUTICAL CONTROLS"**

RESULTS: APPROVED ☒ REJECTED ☐

NOTES: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

SIGNATURE: \_\_\_\_\_ [signature] \_\_\_\_\_ DATE: 30/11/2001